Initially, it is noted that claims 27-46 were renumbered as claims 29-48. It is unclear to applicants why this action has been taken. The Amendment under 37 CFR 1.116 filed on December 20, 1996, which added claims 27 and 28, was denied entry by the Examiner via the Advisory Action of January 23, 1997. See Paper Number 9. Thus, if the amendment was not entered, it appears that the subsequent Amendment of April 26, 2002 was appropriate in the filing of new claims numbered as 27-46.

The rejection of claims 27-46 under 35 U.S.C. 103 (a) as being unpatentable over the teachings of EPA 0,184,162 in view of Johnson (U.S.P.N. 4,411,893) and Showalter (U.S.P.N. 4,556.654) is respectfully traversed. It is the Examiner's position that EPA '162 describes applicants' compounds, as well as the use of those compounds, "as an antimicrobial agents to be applied with a "cancer" (sic) (e.g. carrier) externally i.e. topically." It is further submitted that the "prior art is well aware of how antimicrobial agents are applied topically using lotion, gels and creams" as shown by Johnson and Showalter.

Applicants' respectfully disagree with the Examiner's interpretation of EPA's '162 "external administration" as being synonymous/interchangeable with the instant "topical application." The present claims are directed to *topical compositions of compounds wherein the topical administration of these compounds produces a local effect (i.e. an effect at the site of administration on the skin).* These topical compositions are used to treat "local conditions", e.g. psoriasis, dermatitis, urticaria, etc. **(see page 3 of specification)** without significant penetration through the skin and into the bloodstream.

In contrast, EPA '162 includes *compositions containing active compounds in which the external administration of the compounds yields a systemic effect (i.e. an effect distant from the site of administration on the skin).* It is not the intention of EPA '162 to externally administer compounds to yield a local effect (e.g. an effect on the skin). These external compositions are used to treat "systemic" conditions at a distant site, which is to say they result in a systemic effect, e.g. prevention of resistance by transplantation, treatment of graft versus host disease, auto-immune diseases etc. (see page 66, line 33 through page 67, line 6). It is difficult to imagine that these conditions would be effectively treated by a "local" effect to the skin. Those conditions call for systemic administration of active agents, which may be accomplished via an "external" route such as intranasal, buccal, rectal, etc.

It is requested that the examiner note that all *in vivo* tests given in EPA'162 refer to systemic application (page 71, line 15 to page 76, line 8). Additionally, the specification, on page 76, lines 32-34, states that "[F]or applying this composition to humans, it is preferable to apply it by parenteral or enteral administration." Moreover, the indication "**systemic** Lupus erythematosus" (page 67, line 3) is an inflammatory autoimmune disease that has –as its name indicates – predominantly systemic implications and is definitely not limited to the skin (see e.g. The Merck Manual of Diagnosis and Therapy [1992] 16th edition, p. 1317-1320). This disease is therefore treated systemically (see pages 1319 and 1320). Copy enclosed for the convenience of the Examiner.

Finally, it is noted that nowhere in EPA' 621 is a gel cream or lotion specifically mentioned. While Johnson and Showalter do teach gels, creams, and lotions, neither reference can compensate for the fact that EPA '621 does not teach topical compositions to treat "local" conditions.

In view of the foregoing, it is respectfully submitted that the compositions of claims 29-48are patentable over EPA '621 in view of Johnson and Showalter.

Respectfully submitted,

D. Gabrielle Brouillette

Novartis Corporation
Patent and Trademark Dept.
564 Morris Avenue
Summit, NJ 07901-1027
(908) 522-6720

D. Gabrielle Brouillette
Agent for Applicants
Reg. No. 51,384

Date: August 26, 2002

Encl.: Copy of Merck Manual pp 1317-1321,as indicated